Mixtures of Arsenic, Cadmium, Chromium, and Lead

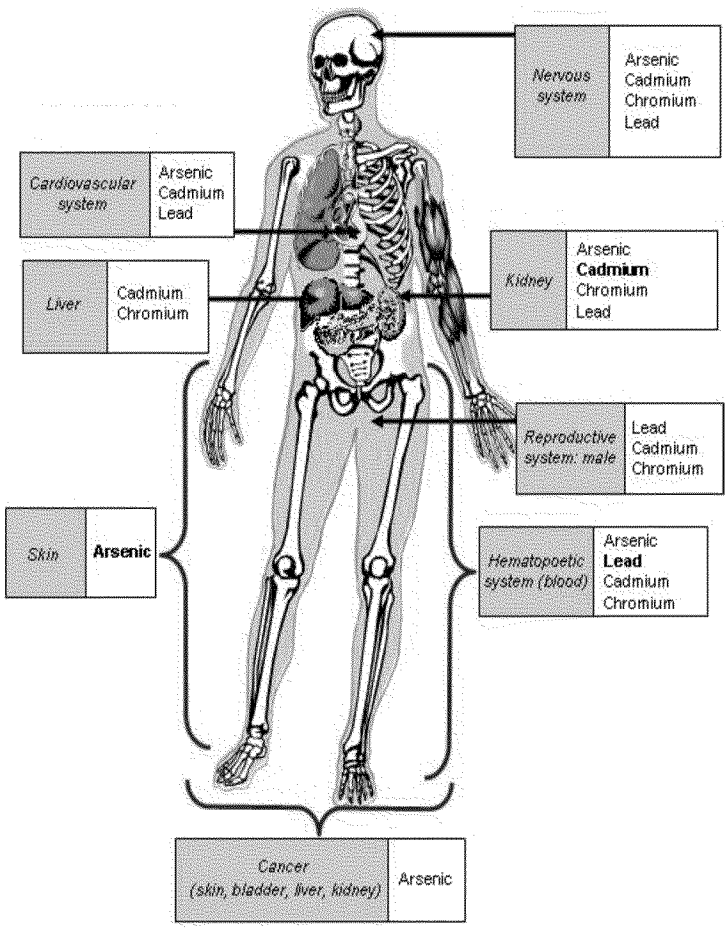
(This fact sheet summarizes information for combinations of metals in this set, with a focus on ingestion of inorganic forms, to support analyses at contaminated sites. Companion fact sheets provide chemical-specific information on common use, general environmental levels, and toxicity, also by other routes.)

Do These Metals Naturally Coexist? Arsenic, cadmium, chromium, and lead all occur naturally in the environment and are found in all materials – soils, plants, animals, and humans – typically as salts. These metals cannot be destroyed, nor do they degrade; however they can be converted to organic forms by biological action both in the environment and within the body. (This fact sheet focuses on inorganic forms.)

What Common Uses Could Result in a Combined Presence? These metals share many industrial uses, including in metallurgy. Arsenic and cadmium are byproducts of lead production, and various combinations are used in materials and processes as highlighted at right. The Agency for Toxic Substances Disease Registry (ATSDR) has identified these four metals as soil contaminants at about 15% of the waste sites reviewed. Amounts and proportions of each vary in content and concentration across different sites.

Uses	Combinations
Metal products, alloys	All four
Dyes, pigments, paints	Chromium, cadmium, lead
Batteries	Cadmium; lead and arsenic
Anti-corrosion/rust coat	Chromium and arsenic
Solder	Lead and arsenic
Wood preservative	Arsenic and chromium

What Health Effects Are Indicated? Chronic oral exposures often represent a route of concern for contaminated sites as contaminants can migrate to groundwater over time. Thus, this fact sheet focuses on ingestion-related effects. Key organs or systems affected by intermediate (subchronic) to long-term (chronic) oral exposures to the individual metals are highlighted at right. Shown are the critical organs and systems (where the first adverse effect is observed, in bold) and those affected at higher levels that are common across two or more metals, or that are known to be affected by another metal in the mixture. (No critical effect has been defined for chromium by the oral route; the respiratory system is the primary target for inhalation.)



Primary Organs/Systems Affected Following Ingestion

What Are The Joint Toxicities? Joint toxicity refers to the outcome of two or more chemicals acting together; three categories of joint toxicity are: greater than additive (synergism and potentiation); additive (no interaction); and less than additive (antagonism and inhibition). Additivity is the default assumption for evaluating health effects of multiple chemicals. Toxicological interactions can either increase or decrease

the apparent toxicity of a mixture relative to that expected from simple addition. No specific health study has been conducted for the quaternary mixture of arsenic, cadmium, chromium, and lead. A few studies have investigated the effects of three metals in combination, but most have studied pairs within this set. The lead-cadmium pair has been studied most, including in human epidemiological studies and oral animal studies. Data from key studies as given in the ATSDR interaction profile are summarized in the table below. These data reflect higher exposures than environmental levels.

Joint Toxicity for Selected Organ/System Endpoints Following Ingestion

Endpoint	*Arsenic* on			*Cadmium* on			*Chromium* on			*Lead* on		
	Cd	Cr	Pb	As	Cr	Pb	As	Cd	Pb	As	Cd	Cr
Nervous system			↑			↑				↑	↔	
Kidney	↔	↓	↓	↔	↔	↓	↓	↔		↓	↔	
Hematological system	↓		↓	↓		↓				↓	↔	
Reproductive: male	↓			*na*		↑	*na*			*na*	↑	
Skin	*na*	*na*	*na*		*na*	*na*	↑	*na*	*na*		*na*	
Cancer	*na*	*na*	*na*		*na*	*na*	↑	*na*	*na*		*na*	*na*

As = arsenic, Cd = cadmium, Cr = chromium, Pb = lead; ↑ = interactive effects are more than additive or one metal enhances an effect induced only by the other metal; ↓ = interactive effects are less than additive or one metal protects against an effect induced only by the other metal; ↔ = results are inconclusive or do not suggest that effects are more or less than additive; blank = relevant information is not available; na = not applicable because oral exposure to this metal is not indicated to cause that health endpoint. Note that for the cardiovascular system, results were inconclusive or unavailable for all pairs.

For neurological effects, the predicted direction of joint toxic action for the mixture is greater than additive for several pairs (arsenic-lead, cadmium-lead, lead-arsenic), which indicates the health hazard of those mixtures might be somewhat greater than that estimated by endpoint-specific hazard indices for this endpoint; the same higher-than-additive effect is indicated for the male reproductive system (testes) for cadmium and lead acting on each other. In contrast, for effects on the kidney and blood, the predicted direction of joint toxic action is less than additive for several metal pairs, indicating that the health hazard might be somewhat less than estimated by endpoint-specific hazard indices.

What Is the Joint Risk? No specific data exist to quantify the joint risk of mixtures of arsenic, lead, cadmium and chromium. Endpoints of potential concern for this mixture include critical effects of the individual metals as well as the common targets of toxicity that might become significant due to additivity (considering secondary effects) or certain interactions, as indicated in the table above (noting again that additional interactions protect against other adverse effects). The ATSDR recommends using a hazard index method with the target-organ toxicity dose (TTD) modification and qualitative weight-of-evidence (WOE) method to assess the additive and interactive actions of the mixture components. These methods are suggested only when exposures are significant, i.e., only if the hazard quotients for two or more metals are 0.1 or greater. If only one or none of the metals have a hazard quotient at or above that level, then no further assessment of joint toxic action is needed because additivity and/or interactions are unlikely to result in a significant health hazard.

Where Can I Find More Information? More information can be found in the primary information source for this overview, the interaction profile for arsenic, cadmium, chromium and lead prepared by ATSDR (http://www.atsdr.cdc.gov/interactionprofiles/ip04.html). Additional information can be found in the companion fact sheets for each of these metals and their respective information sources.